# Concurrent chemoradiation for muscle-invasive bladder cancer using 5-fluorouracil vs. capecitabine: a nationwide cohort study

Amy de Haar-Holleman*, **Lisa M.C. van Hoogstraten***, Maarten C.C.M. Hulshof, Metin Tascilar, Katharina Brück, BlaZIB study group, Richard P. Meijer, J. Alfred Witjes, Lambertus A. Kiemeney, Katja K.H. Aben

Global congress on bladder cancer | 21 October 2022

# Conflicts of interest

- None to disclose

# Chemoradiotherapy for muscle-invasive bladder cancer

- Chemoradiotherapy (CRT)
  - Bladder-preserving alternative to radical cystectomy
  - RT + chemotherapy as radiosensitizer
  - Ideal CRT regimen not yet determined
    - Type of chemosensitizer varies between geographical regions in NL

# Capecitabine as an alternative to 5-fluorouracil

- **5-FU (+ MMC)**
  - Intravenous administration + associated risks
  - Chemotherapy requires hospital admission
  - Regular hospital visits for RT



- **Capecitabine (+ MMC)**
  - Prodrug generating 5-FU preferentially within tumor
  - Oral administration (tablets)
  - Drug intake at home
  - Less hospital visits



→ More patient-friendly

→ Replace 5-FU?

# Objective

- To evaluate toxicity, overall and disease-free survival of **5-FU (+ MMC)** versus **capecitabine (+ MMC)** in patients with MIBC using real world data

# Patient selection

- Netherlands Cancer Registry
  - MIBC (cT2-T4a N0/1/2/x M0/x)
  - Urothelial carcinoma
  - Diagnosis between November 2017 and November 2019
  - Treated with CRT



5-FU + MMC (N=111)



Capecitabine + MMC (N=111)

- Additional data collection within BlaZIB study*

**Ripping et al., 2020. BMC Cancer*

# Patient and tumor characteristics largely comparable

- No difference regarding:
  - Gender, age, comorbidities, BMI
- Patients in capecitabine group had:
  - Better performance status
  - Higher socioeconomic status
  - Lower disease stage

| | 5-FU + MMC | Capecitabine + MMC |
|---|---|---|
| **Performance status** | | |
| ECOG 0 | 50 (45.0%) | 66 (59.5%) |
| ECOG 1 | 45 (40.5%) | 35 (31.5%) |
| ECOG 2 or higher | 16 (14.4%) | 10 (9.0%) |
| **Socioeconomic status** | | |
| Low | 36 (32.4%) | 20 (18.0%) |
| Middle | 47 (42.3%) | 40 (36.0%) |
| High | 28 (25.2%) | 51 (45.9%) |
| **Disease stage (cTNM)** | | |
| cT2N0M0 | 71 (64.0%) | 90 (81.1%) |
| cT3-T4aN0M0 | 37 (33.3%) | 17 (15.3%) |
| cTanyN+M0 | 3 (2.7%) | 4 (3.6%) |

# Treatment compliance and toxicity

- **5-FU (+ MMC)**
  - 62% complied to curative protocol
    - Mostly 66 Gy in 33 fractions
  - Toxicity* reported in 21% (n=23)
    - Mostly hematological (n=8)



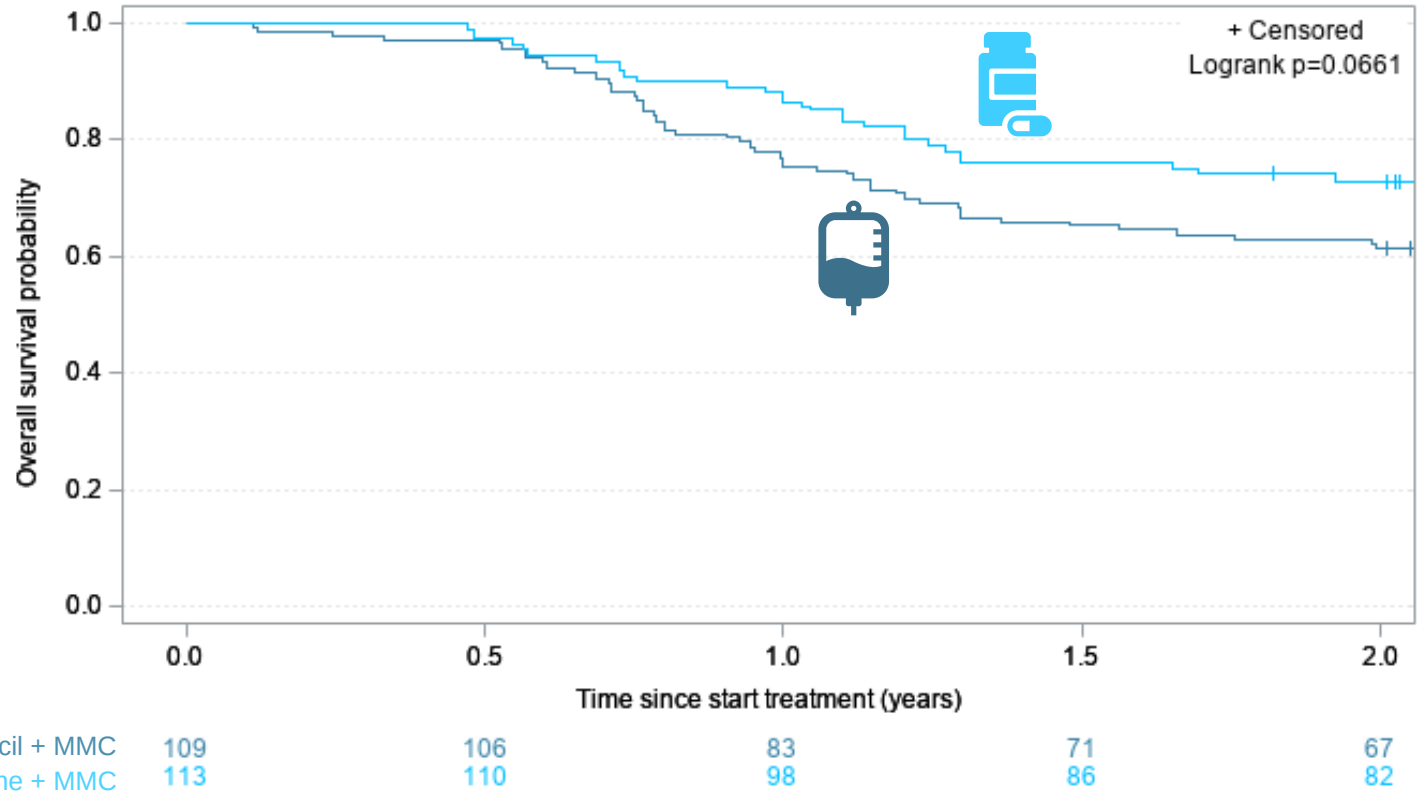
- **Capecitabine (+ MMC)**
  - 77% complied to curative protocol
    - Mostly 60 Gy in 25 fractions
  - Toxicity* reported in 14% (n=16)
    - Mostly hematological (n=6)



*Toxicity defined as: adjustment of CRT schedule, complications (CTCAE ≥3) or readmission to hospital due to CRT

# Overall survival appeared in favor of capecitabine

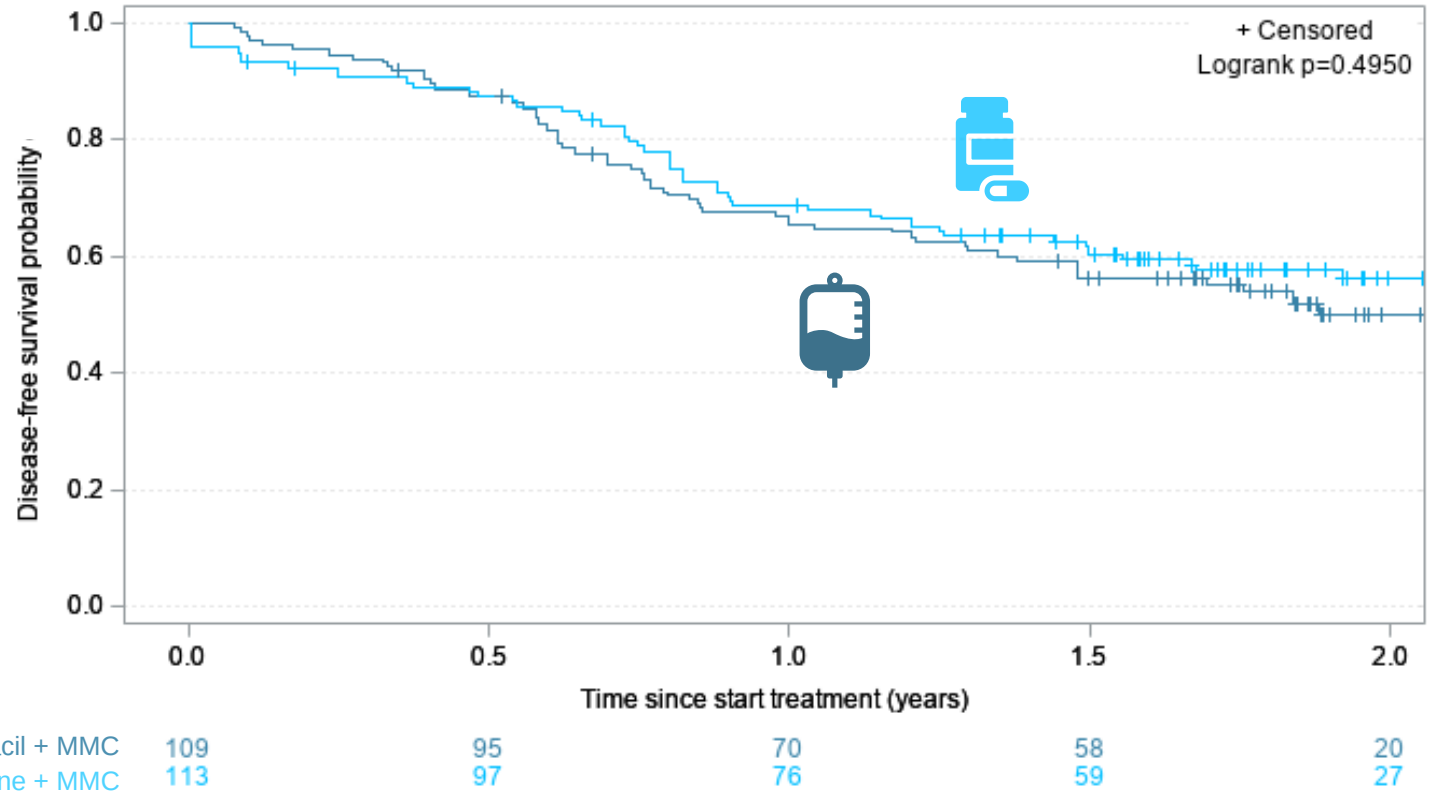
- 2-year adjusted* overall survival
  - 5-FU vs. capecitabine:
  - 61% vs. 73% (p=0.07)




*Inverse probability treatment weighting (IPTW), based on performance status, disease stage, socioeconomic status

# No significant difference in disease-free survival

- 2-year adjusted* disease-free survival
  - 5-FU vs. capecitabine:
  - 50% vs. 56% (p=0.50)




*Inverse probability treatment weighting (IPTW), based on performance status, disease stage, socioeconomic status

# Discussion

- Limitations
  - Potential underreporting of toxicity
  - Confounding by unmeasured factors?

- Strengths
  - First to compare 5-FU and capecitabine in unselected, nationwide population
  - High-quality, real-world data

# Conclusions

In chemoradiotherapy for MIBC…

| | 5-fluorouracil (+ MMC) | | Capecitabine (+ MMC) |
|---|---|---|---|
| • Toxicity |  | = |  |
| • Survival (OS & DFS) |  | = |  |
| • Patient-friendly |  | < |  |

 Our data support replacement of 5-FU by capecitabine

# Acknowledgements

**BlaZIB study group:**

**Urologists**
- Joost Boormans, Erasmus Medical Centre
- Catharina A. Goossens-Laan, Alrijne hospital
- Antoine G. van der Heijden, Radboud UMC
- Tom J.N. Hermans, VieCurie Medical Centre
- Anna M. Leliveld, UMC Groningen
- Richard P. Meijer, UMC Utrecht
- Reindert J.A. van Moorselaar, Amsterdam UMC
- Jorg R. Oddens, Amsterdam UMC
- Theo M. de Reijke, Amsterdam UMC
- Bas W.G. van Rhijn, Netherlands Cancer Institute - AvL
- Joep G.H. van Roermund, Maastricht UMC
- Bart P. Wijsman, Elisabeth-TweeSteden Ziekenhuis
- J. Alfred Witjes, Radboud UMC

**Radiotherapists**
- Maarten C.C.M. Hulshof, Amsterdam UMC
- Juus L. Noteboom, UMC Utrecht

**Pathologists**
- Geert J.L.H. van Leenders, Erasmus Medical Centre

**Patient representatives**
- Sipke Helder, Patient association 'Leven met blaas- of nierkanker'
- Guus W.J. Venderbosch, Patient association 'Leven met blaas- of nierkanker'

**Medical oncologists**
- Michiel S. van der Heijden, Netherlands Cancer Institute
- Sasja F. Mulder, Radboud UMC
- Tineke J. Smilde, Jeroen Bosch Hospital

**Epidemiologists**
- Theodora M. Ripping, Netherlands Comprehensive Cancer Organisation
- Lambertus A.L.M. Kiemeney, Radboud UMC
- Katja K.H. Aben, Netherlands Comprehensive Cancer Organisation

The BlaZIB study is funded by: KWF Kanker Bestrijding

# Thank you for your attention!

l.vanhoogstraten@iknl.nl

www.blazib.nl

https://www.linkedin.com/in/lisa-van-hoogstraten/